Gas-Phase Chemistry

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Efficient and Selective Gas-Phase Monomethylation versus N–H Bond Activation of Ammonia by "Bare" $Zn(CH_3)^+$: Atomic Zinc as a Leaving Group in an S_N2 Reaction**

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Dedicated to Professor Bernd Brutschy on the occasion of his 65th birthday

As a consequence of the key positions that the elements nitrogen and carbon occupy in nature, C–N bond formation constitutes an important issue in biological and industrial processes.[1] While the large-scale synthesis of hydrogen cyanide by the Degussa and Andrussow procedures (by employing ammonia and methane) is well established, other compounds containing carbon and nitrogen are synthesized in more complex reaction sequences.[2] The simplest entities containing C–N single bonds are methylamine (MA), dimethylamine (DMA), as well as trimethylamine (TMA); they are produced in exothermic reactions of ammonia and methanol in the presence of dehydration catalysts.[3] As the thermodynamically favored product TMA is of only minor commercial interest, quite some research efforts have been made to control and improve the selectivity of the synthesis of MA and DMA.[4] Currently, zeolites are commonly employed in the industrial amination of alcohols, and several mechanisms have been suggested.[5] Unfortunately, these catalysts do not provide the required selectivity; consequently, other catalytic systems, for example, carbon-based compounds[4d] and transition-metal-doped hydrotalcites,[4e,6] have been investigated. In the latter case, copper is often used as a dopant element; this is not surprising given the well-known C–N Ullmann-type coupling reactions.[7] So far, zinc-based compounds play an imperceptible role in C–N bond formation; however, the first investigations in this field date back to 1884, when zinc chloride was used as a dehydrating agent.[8]

Several systems that bring about C–N bond formation have been studied in gas-phase experiments, which provide an ideal arena to address mechanistic aspects:[9]

a) In the reaction of $Pt(CH_2)^+$ with ammonia, three different product ions are formed [Eqs. (1)–(3)] in the ratio 14:5:1.[10]

$$Pt(CH_2)^+ + NH_3 \rightarrow CH_2NH_2^+ + PtH \quad (1)$$

$$Pt(CH_2)^+ + NH_3 \rightarrow Pt[CH(NH_2)]^+ + H_2 \quad (2)$$

$$Pt(CH_2)^+ + NH_3 \rightarrow NH_4^+ + PtCH \quad (3)$$

b) Platinum-based heteronuclear clusters of the type $PtM(CH_2)^+$ (M = Cu, Ag, Au) also mediate carbon–nitrogen coupling [Eq. (4)], as revealed by labeling experiments.[11]

$$PtM(CH_2)^+ + NH_3 \rightarrow PtM[CH(NH_2)]^+ + H_2 \ (M = Cu, Ag, Au) \quad (4)$$

In contrast, no C–N bond formation brought about by ligated or "bare" first-row transition-metal ions in the reaction with NH_3 has been reported.[10b] Here, we will describe the first example. The special bonding pattern of ligated zinc ions comes along with a rather high bond-dissociation energy, $BDE(Zn^+\text{-}CH_3) = 280 \pm 4\ kJ\,mol^{-1}$,[12] and a remarkably low one for $Zn(OH)^+$, $BDE(Zn^+\text{-}OH) = 127\ kJ\,mol^{-1}$.[13] The latter value points to the inability of zinc cations to form multiple bonds due to the absence of empty d-orbitals; in addition, the repulsive interaction of the closed d-shell with the lone pairs of electrons on the oxygen atom weakens the metal–oxygen bond.[14] Considering the general trend of stronger M–O bonds in $M(OH)^+$ compared to the M–N bonds in $M(NH_2)^+$, with M being a first-row transition metal,[13,15] $BDE(Zn^+\text{-}NH_2)$ is assumed to be lower than $BDE(Zn^+\text{-}OH)$; thus, N–H bond activation of ammonia by $Zn(CH_3)^+$ to generate in a ligand-switch reaction $Zn(NH_2)^+$ and CH_4 would most likely be endothermic and thus not possible under thermal conditions.[16] However, this situation may be beneficial for other reaction channels of the $Zn(CH_3)^+/NH_3$ system, including C–N coupling processes.

As shown in Figure 1, the thermal reaction of mass-selected $Zn(CH_3)^+$ with ammonia gives rise to two products [Eqs. (5) and (6)] with a branching ratio of 5.3:1. A ligand-switch [Eq. (7)] does not take place.

$$Zn(CH_3)^+ + NH_3 \rightarrow CH_3NH_3^+ + Zn \quad (5)$$

$$Zn(CH_3)^+ + NH_3 \rightarrow Zn(CH_3)(NH_3)^+ \quad (6)$$

$$Zn(CH_3)^+ + NH_3 \not\rightarrow Zn(NH_2)^+ + CH_4 \quad (7)$$

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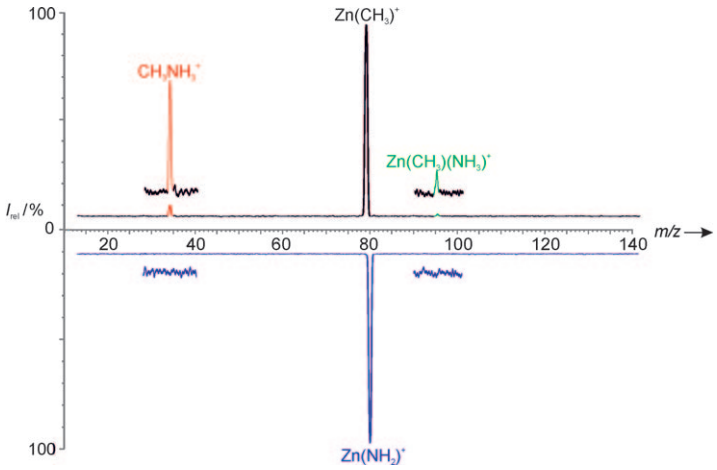

Figure 1. Ion/molecule reactions of mass-selected $Zn(CH_3)^+$ with ammonia (upper part) and $Zn(NH_2)^+$ with methane (lower part, mirrored at the base line) under thermal conditions. Important regions are enlarged by a factor of 10.

The assignment of the two channels is further supported by labeling experiments with the couples $Zn(CH_3)^+/ND_3$, $Zn(CD_3)^+/NH_3$, and $Zn(CD_3)^+/ND_3$.[17]

The rate coefficient for the system $Zn(CH_3)^+/NH_3$ amounts to 9.9×10^{-10} cm^3 s^{-1} molecule^{-1}; this corresponds to an efficiency of 54% relative to the gas-kinetic collision limit (Figure 2).[18] The observation of reaction (5) is in line with reported thermochemical data with higher values of the methyl-cation affinity: $MCA(NH_3) = 446$ kJ mol^{-1} compared to $MCA(Zn) = 332$ kJ mol^{-1}.[19] Additionally, adduct formation [Eq. (6)] is confirmed by a change of the branching ratio in preference for $Zn(CH_3)(NH_3)^+$ at higher pressures.

As shown in Figure 1 (bottom), no thermal reaction between $Zn(NH_2)^+$ and methane [Eq. (8)] is observed at the

$$Zn(NH_2)^+ + CH_4 \not\rightarrow Zn(CH_3)^+ + NH_3 \qquad (8)$$

detection limit; this is surprising considering the high BDE of Zn^+-CH_3 compared with the estimated low BDE of Zn^+-NH_2

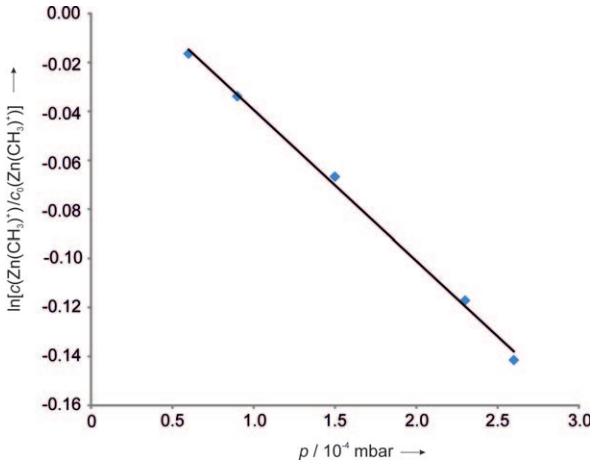

Figure 2. Plot of ln (c[$Zn(CH_3)^+$]/c_0[$Zn(CH_3)^+$]) versus ammonia pressure for the thermal reaction of $Zn(CH_3)^+$ with NH_3 ($R^2 = 0.9971$).

mentioned above. While C–H bond activation of CH_4 accompanied by loss of ammonia should be feasible from a thermodynamic point of view, its absence points to the presence of a kinetic barrier.

Calculations were performed to obtain further mechanistic insights into the C–N coupling reaction [Eq. (5)], as well as to the origin of the non-occurrence of reactions (7) and (8); only singlet states have been considered, as they correspond to the electronic ground states for all the transition structures and species involved in the reactions.[22] The related triplet states are so much higher in energy (e.g. $Zn(CH_3)^+$ 210.3 kJ mol^{-1}) that they do not need to be considered for thermal reactions. As shown in Figure 3a, N–H bond activation in the couple $Zn(CH_3)^+/NH_3$ is both endothermic and inhibited by a high energy barrier ($\mathbf{TS_{1a/2}}$); the latter one also impedes the back reaction [Eq. (8)], that is, C–H bond activation of CH_4 in the $Zn(NH_2)^+/CH_4$ couple, despite the exothermicity of this reaction channel. Two pathways were identified (Figure 3b) for the C–N bond formation [Eq. (5)]. Starting from the linear encounter complex $(CH_3)Zn(NH_3)^+$ (**1a**), formation of $CH_3NH_3^+$ is inhibited by an energetically rather demanding transition structure ($\mathbf{TS_{1a/3a}}$), in which zinc mediates the reductive coupling of the two ligands. While the overall process, relative to the entrance channel is exothermic

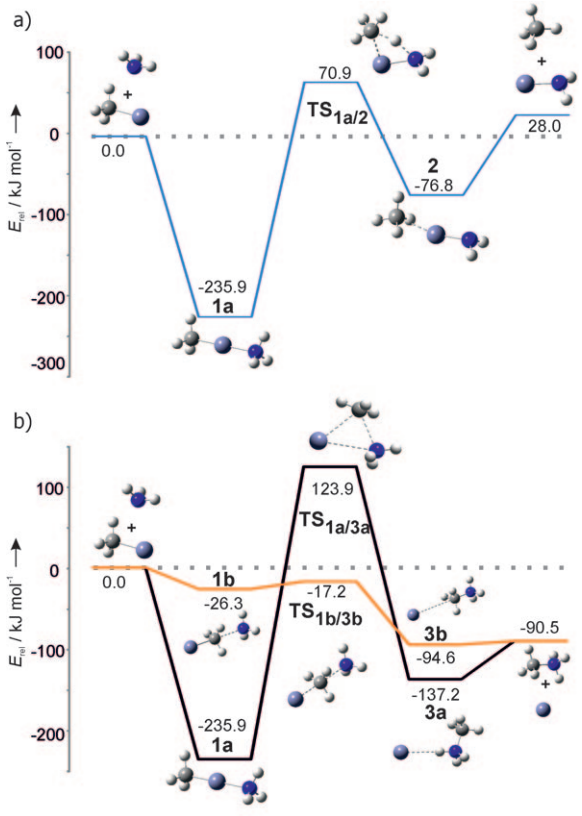

Figure 3. Potential-energy surfaces for the singlet ground state of the $Zn(CH_3)^+/NH_3$ couple calculated at the UCCSD(T)/def2-QZVP//UB3LYP/def2-QZVP level of theory: a) N–H bond activation to form $Zn(NH_2)^+$ and CH_4; b) C–N bond formation to provide $CH_3NH_3^+$/Zn.

($-90.5\ kJ\,mol^{-1}$), it is not accessible under thermal conditions; rather, the reactants are trapped as an adduct complex [**1a**; Eq. (6)]. However, C–N bond formation can be achieved by a direct, S_N2-type interaction between the methyl ligand and the NH_3 substrate. Here, the intermediate $Zn(CH_3)(NH_3)^+$ (**1b**) is formed by coordination of NH_3 to the methyl carbon atom as the first step. Subsequently, the C–Zn bond gets elongated and, with a small energy barrier of only $9.1\ kJ\,mol^{-1}$, the nucleophilic substitution product **3b** is generated via $\mathbf{TS_{1b/3b}}$. Intermediate **3b** corresponds to a weakly bound ion–neutral complex[23] of a neutral zinc atom and $CH_3NH_3^+$; the latter can easily decompose to atomic zinc and protonated methylamine ($CH_3NH_3^+$). In this reaction, the methyl group in $Zn(CH_3)^+$ acts as an electrophilic ligand and the Zn atom as a leaving group;[24] this behavior is in distinct contrast to the model system of carbonic anhydrase $Zn(L)_n(OH)^+$ (L = imidazole, pyridine, phenanthroline; n = 0–3), in which the presence of the nucleophilic ligand OH is essential for the CO_2 activation, as observed in gas-phase experiments.[25] The different behavior of the two Zn complexes is reflected in the calculated charge distributions; based on natural population analyses (B3LYP/6-311++G(d,p)) these are 0.78 and 0.22 for Zn and CH_3, respectively, in $Zn(CH_3)^+$, and 1.56 and −0.56 for Zn and OH, respectively, in $Zn(OH)^+$.[25,26] The electrophilic nature of the methyl group of $Zn(CH_3)^+$ and its relationship to a methyl cation is also indicated in the sum of the ∡HCH angles (343.3°) compared with 360° in CH_3^+ and 329° in ethane. Formation of "bare" Zn^+ as an alternative decomposition path of **3b** is calculated to be endothermic by $380.5\ kJ\,mol^{-1}$; this is in line with a 2.4-fold higher ionization energy (IE) of zinc compared with that calculated for CH_3NH_2.[21c,27] Also the formation of methylamine and cationic ZnH^+ is calculated to be endothermic by $125.1\ kJ\,mol^{-1}$. The generation of $CH_3NH_3^+$ from $Zn(CH_3)^+/NH_3$ constitutes an unusual S_N2-type gas-phase reaction in so far as an atomic element (Zn) serves as a leaving group. Although the enthalpy barriers of gas-phase S_N2 reactions are often low, the rate constants can be rather small, due to entropic factors that may play a prominent role in this ubiquitous reaction. This point as well as the problems of describing these reactions with DFT-based methods have been addressed at quite some length from both experimental and computational points of view.[28,29]

Table 1 summarizes selected bond lengths of all the structures given in Figure 3; they are in good agreement with data calculated previously for $Zn(CH_3)^+$ and $CH_3NH_3^+$.[20,30]

In summary, in this combined experimental/theoretical study, we have demonstrated that C–N bond formation from the reaction of $Zn(CH_3)^+$ with NH_3 is possible under thermal conditions; this reaction does not take place in the $Zn(NH_2)^+/CH_4$ system. The coupling [Eq. (5)] proceeds through an S_N2-type gas-phase mechanism. Furthermore, N–H bond activation in $Zn(CH_3)^+/NH_3$ as well as C–H bond activation in $Zn(NH_2)^+/CH_4$ are prohibited by kinetic barriers.

Table 1: Selected bond lengths (r) in Å of species shown in Figure 3.

	r(C-Zn)	r(N-Zn)		r(C-Zn)	r(N-Zn)	r(C-N)
$Zn(CH_3)^+$	2.001	–	$\mathbf{TS_{1a/3a}}$	2.726	3.123	2.380
1a	1.930	2.016	**3a**	–	2.574	1.506
$\mathbf{TS_{1a/2}}$	2.157	1.923	**1b**	2.113	–	2.529
2	2.219	1.808	$\mathbf{TS_{1b/3b}}$	2.240	–	2.319
$Zn(NH_2)^+$	–	1.856	**3b**	3.969	–	1.515
			$CH_3NH_3^+$	–	–	1.512

Experimental Section and Methods

The experiments were performed with a VG BIO-Q mass spectrometer of QHQ configuration (Q: quadrupole, H: hexapole) equipped with an ESI source, as described in detail elsewhere.[31] Millimolar solutions of $Zn(O_2CCH_3)_2(H_2O)_2$ and $Zn(O_2CCD_3)_2$ in pure methanol/[D_4]methanol as well as $ZnCl_2$ in formamide were introduced through a fused-silica capillary to the ESI source with a syringe pump (ca. 4 μL min^{-1}). As revealed by parent-ion scans, in which precursor ions could be identified,[32] the $Zn(CH_3)^+$ ion was generated in the ESI source from carboxylate ions of the type $Zn_2(O_2CCH_3)_n(OH)_{3-n}^+$ (n = 1–3), by collision-induced dissociation under the loss of CO_2, C_2H_2O, as well as $Zn(OH)_2$.[33] For $Zn(NH_2)^+$, $Zn(formamide)_3^{2+}$ was identified as the parent ion, as described before for similar systems.[34] The degree of dissociation of the precursor ions, as a result of collisions with N_2 which was used as a drying gas in the ESI source, was determined by the cone voltage; maximal yields of the desired complexes were achieved by adjusting the cone voltage to around 50–80 V. The identity of the ions was confirmed by comparison with the expected isotope patterns.[35] The ion/molecule reactions of the mass-selected cationic complexes with the substrates were probed at a collision energy (E_{lab}) set nominally to 0 eV, which in conjunction with the ca. 0.4 eV kinetic energy width of the parent ion at half peak height allows the investigation of quasithermal reactions, as demonstrated previously.[25,36] The error of the absolute rate coefficients was assumed to be ±50% which is also reflected in the non-zero crossing of the graph in Figure 2. That might be due to different sensitivity of the gauge at different pressures.

Calculations were performed with the Gaussian09 program package[37] using def2-QZVP basis sets[38] and the unrestricted B3LYP level of theory[39] for geometry optimizations and frequency calculations, to verify stationary points and transition states, and the unrestricted CCSD(T)[40] level for selected single-point calculation. All energies (given in kJ mol^{-1}) were corrected for (unscaled) zero-point vibrational energy contributions obtained with UB3LYP/def2-QZVP. Intrinsic reaction coordinate (IRC) calculations were performed to link transition structures with the corresponding minima.[41]

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